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Occurrence of epileptiform discharges and sleep during EEG recordings in children after melatonin intake versus sleep-deprivation

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HIGHLIGHTS

- The occurrence rate of epileptiform discharges in the EEG of children 1–16 years of age does not differ in sleep induced by melatonin and sleep deprivation.
- Melatonin is equally efficient as partial sleep deprivation in inducing sleep.
- Melatonin may be preferable in younger children as they fall asleep easier than after partial sleep deprivation, and also from the parent's perspective.

ABSTRACT

Objective: To determine if melatonin is equally efficient as partial sleep deprivation in inducing sleep without interfering with epileptiform discharges in EEG recordings in children 1–16 years old.
Methods: We retrospectively analysed 129 EEGs recorded after melatonin intake and 113 EEGs recorded after partial sleep deprivation. Comparisons were made concerning occurrence of epileptiform discharges, the number of children who fell asleep and the technical quality of EEG recordings. Comparison between different age groups was also made.
Results: No significant differences were found regarding occurrence of epileptiform discharges (33% after melatonin intake, 36% after sleep deprivation), or proportion of unsuccessful EEGs (8% and 10%, respectively). Melatonin and sleep deprivation were equally efficient in inducing sleep (70% in both groups). Significantly more children aged 1–4 years obtained sleep after melatonin intake in comparison to sleep deprivation (82% vs. 58%, $p \leqslant 0.01$), and in comparison to older children with melatonin induced sleep (58–67%, $p \leqslant 0.05$). Sleep deprived children 9–12 years old had higher percentage of epileptiform discharges (62%, $p \leqslant 0.05$) compared to younger sleep deprived children.
Conclusion: Melatonin is equally efficient as partial sleep deprivation to induce sleep and does not affect the occurrence of epileptiform discharges in the EEG recording. Sleep deprivation could still be preferable in older children as melatonin probably has less sleep inducing effect.
Significance: Melatonin induced sleep have advantages, especially in younger children as they fall asleep easier than after sleep deprivation. The procedure is easier for the parents than keeping a young child awake for half the night.

1. Introduction

One of the cornerstones in the diagnosis of epilepsy in children is the results from electroencephalography (EEG). Performing EEG recordings in young children may, however, be challenging since a good quality requires that the patient does not move. Therefore, the method of choice so far has been EEG performed during sleep. Sleep also improves the sensitivity of the examination, by increasing the amount of epileptiform activity in the EEG (Niedermeyer and Lopes da Silva, 2005a). Natural sleep is desirable since many pharmacological agents influence brain activity and as a consequence decrease the occurrence of epileptiform discharges

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(Ashrafi et al., 2010; Niedermeyer and Lopes da Silva, 2005a). Many neurophysiology clinics use sleep deprivation to obtain reliable recordings (Degen, 1980; Giorgi et al., 2013; Leach et al., 2006; Wassmer et al., 1999). The incidence of epileptiform discharges in sleep deprived EEGs does, however, vary widely from 32% to 72% in different reports (Marinig et al., 2000). Furthermore, sleep deprivation is not easy to achieve in young children and could be burdensome for both children and parents. Therefore melatonin, given prior to the investigation, is currently used in a number of laboratories to induce sleep before the EEG recording (Eisermann et al., 2010; Sander et al., 2012; Wassmer et al., 2001a,b).

Melatonin is a hormone produced in the pineal gland. It regulates circadian rhythms and some aspects of the sleep–wake cycle. It is widely used to treat jet lag and sleep disturbances (e.g. sleep onset delay) (Cortese et al., 2013; Herxheimer and Petrie, 2002). During the last two decades, studies reporting a sleep inducing effect of melatonin (Wassmer et al., 2001a; Milstein et al., 1998), as well as its safety in children (i.e., lack of side-effects and tolerability) (Sander et al., 2012) have been published. Melatonin is well tolerated also in children with behavioural problems (Eisermann et al., 2010; Mohammadi et al., 2012; Wassmer and Whitehouse, 2006). Doses of melatonin vary between different studies ranging from 2 mg up to 20 mg (Eisermann et al., 2010; Wassmer et al., 2001a,b), and there is no clear consensus regarding when and in which doses melatonin should be administrated in children. To the best of our knowledge there are no studies that have described the effect of melatonin intake on epileptiform discharges during sleep in different age groups or compared it to the effects of sleep deprivation. The issue of whether to use melatonin or sleep deprivation as a sleep inducer and in which age groups they should be chosen therefore remains controversial (Giorgi et al., 2013; Marinig et al., 2000).

The aim of this study was to determine whether melatonin is equally efficient as partial sleep deprivation in inducing sleep without interfering with epileptiform discharges in EEG in children as well as the technical quality of EEG recordings. We also analysed the sleep inducing effects of melatonin in comparison to partial sleep deprivation, as well as occurrence of epileptiform discharges in EEG recordings in different age groups.

2. Materials and methods

2.1. Subjects and study design

We retrospectively analysed 129 EEG recordings from 121 patients with melatonin induced sleep and 113 EEGs from 111 patients after partial sleep deprivation, aged 1–16 years. The EEGs were performed at a Swedish university hospital during two different time periods: 2010–2011 for melatonin induced sleep and 2007–2008 for sleep deprivation. The routines in our department changed in 2009 when we began to use melatonin in clinical practise to induce sleep in paediatric patients during EEG recordings. Partial sleep deprivation was routinely used before 2009. Children undergoing sleep deprived EEG during 2010–2011 were excluded from further analyses. Patient selection and mean age of the participants are shown in Fig. 1. All children were referred by paediatric neurologists or paediatricians. The indications for EEG were suspected epilepsy, unclear spells, or treatment control in patients with established epilepsy. Reasons for performing sleep EEG in children with established epilepsy were to get an EEG recording without movement artefacts. Clinical background data, such as epilepsy diagnosis, developmental delay and behavioural problems were obtained from referrals, as well as self-reported data from patients and parents documented in the medical records when referred to the EEG recording. EEG recordings were divided into four groups depending of the age of the children (i.e., 1–4 years, 5–8 years, 9–12 years and 13–16 years).

2.2. EEG recordings

For partial sleep-deprived EEGs, caregivers were told to put the child to sleep between 7 p.m. and 9 p.m. the night prior to the examination, and to wake the child at 4 a.m. Sleep deprived EEGs were recorded at 8 a.m. For sleep EEGs using melatonin, children between 1 and 4 years of age were given 3 mg melatonin in liquid form orally and children between 5 and 16 years of age 6 mg, 15 min prior to electrode application. No specific instructions were given regarding prior sleep. These EEGs usually were performed in the early afternoon between noon and 2 p.m.

EEGs were performed using a standard procedure with silver cup scalp electrodes placed according to the international 10–20 system modified adjusted to the patients' age. A Nicolet One EEG Recorder/Reader v.5.30.1.1178 (Copyright 2007 – VIASYS Healthcare Inc.) EEG equipment was used. Electrode impedances were less than 10 kΩ and the high-pass filter was set at 70 Hz. All EEG recordings were performed in a dark and quiet room, and the children were instructed to lie calmly and try to go to sleep. The EEG examination lasted between 30 and 40 min.

EEGs were evaluated by physicians specialised in clinical neurophysiology. All EEGs with epileptiform discharges were re-evaluated by the first author (G.G.). Epileptiform discharges were considered present only if they had well defined morphology and were seen recurrently without influence of muscle or movement artefacts and from electrodes with high conductance. Single isolated epileptiform discharges were not accounted for because of uncertain clinical specificity (Niedermeyer and Lopes da Silva, 2005b). Unsuccessful EEG was defined as either an EEG that was impossible to record due to an uncooperative child or a recording that was difficult to evaluate due to artefacts.

2.3. Statistical analyses

Statistical analyses were performed in Statistica, version 10 (Copyright StatSoft, Inc 1984–2011) and via web-site www.openepi.org. Comparisons were made in three steps. In the first step comparisons were made between melatonin induced sleep and sleep deprived EEGs in children 1–16 years old as a whole group. In the second step comparisons were made between the two EEG modalities (i.e., melatonin induced sleep EEG and sleep deprived EEG) in four different age groups. In the third step comparisons were made between different age groups within each EEG modality. In each step comparisons were made concerning occurrence of epileptiform discharges, the number of children who fell asleep and proportion of unsuccessful EEG recordings.

Statistical analyses of baseline characteristics were performed with chi-square test for categorical variables and Student's t test for continuous variables.

Chi-square test or Fisher's exact test, when appropriate, were used to compare the occurrence of epileptiform discharges and occurrence of sleep and proportion of EEGs that were defined as unsuccessful. Statistical significance was set at $p \leqslant 0.05$.

3. Results

There were no significant differences in the number of EEG recordings showing epileptiform discharges, types of epileptiform activity or occurrence of other abnormalities (i.e., general or focal slowing of background activity) in children between 1 and 16 years of age who received melatonin prior to EEG, as compared to those who were sleep deprived (Table 1). Furthermore, no statistical

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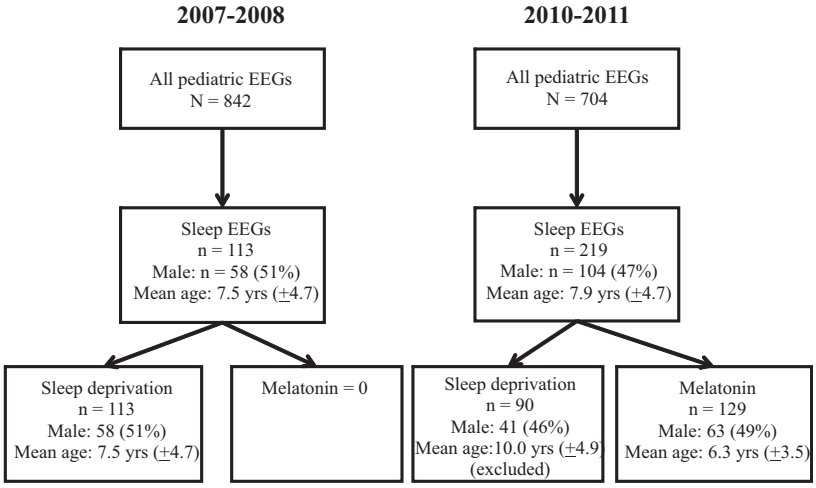

Fig. 1. Flow diagram of EEGs recorded in children 1–16 years of age from 2007 to 2008 and from 2010 to 2011. In the statistical analyses EEGs performed between 2007 and 2008 were compared with melatonin induced sleep EEGs performed between 2010 and 2011.

Table 1
Frequency of epileptiform discharges, abnormalities, normal and unsuccessful EEGs and occurrence of sleep in children, 1–16 years of age, examined with EEG after melatonin induced sleep versus sleep deprivation.

EEG characteristics	Melatonin $n = 129$	Sleep deprivation $n = 113$	p-Value $p \leqslant 0.05$
Epileptiform discharges, in total, n (%)	43 (33)	41 (36)	n.s.
Generalised epileptiform discharges, n (%)	16 (12)	13 (12)	n.s.
Focal epileptiform discharges, n (%)	27 (21)	28 (24)	n.s.
Abnormality, in total, n (%)	16 (12)	15 (13)	n.s.
General abnormality, n (%)	11 (8)	9 (8)	n.s.
Focal abnormality, n (%)	5 (4)	6 (5)	n.s.
Normal EEG, n (%)	60 (47)	51 (45)	n.s.
Sleep obtained, n (%)	90 (70)	79 (70)	n.s.
Unsuccessful EEG, n (%)	10 (8)	11 (10)	n.s.

n.s. = not significant.

significant differences regarding epileptiform activity emerged between melatonin and sleep-deprived EEGs recorded in children from the same age group (Table 2). In the group of sleep deprived children, those who were 9–12 years of age had higher frequency of epileptiform discharges (62%, $p \leqslant 0.05$) in comparison to younger children 1–4 and 5–8 years old who were sleep deprived (Fig. 2). No significant difference in the occurrence of epileptiform discharges was found between age groups among children who got melatonin (Fig. 2).

Overall, the occurrence of sleep after melatonin intake and after sleep deprivation was equal in both groups of children between 1 and 16 years of age (70%, n.s.) (Table 1). Significantly more children between 1 and 4 years of age receiving melatonin prior to the EEG fell asleep in comparison with those of the same age who were sleep deprived ($p \leqslant 0.01$) (Table 2). Also when comparing different age groups of children receiving melatonin prior to EEG, children aged 1–4 years fell asleep easier than children 5–12 years old receiving melatonin prior to EEG ($p \leqslant 0.05$) (Fig. 3). We did not find any difference in obtaining sleep between sleep deprived children from different age groups (Fig. 3).

There was no significant difference between melatonin induced and sleep-deprived EEGs regarding the number of examinations that were defined as unsuccessful (Table 1). Of those EEG recordings with melatonin induced sleep 9 children out of 10 had developmental delay. In the group of sleep deprived children with unsuccessful recordings ($n = 11$) only one child (14 years old) had developmental delay. There were more children with developmental delay in the group receiving melatonin prior to EEG than in the group that was sleep deprived (27 vs. 14), although this difference was not statistically significant.

Overall, there were fewer paediatric EEGs performed 2010–2011 than 2007–2008. A greater proportion of all paediatric EEGs were performed during sleep in 2010–2011 in comparison to 2007–2008 (31% vs. 13%, $p \leqslant 0.001$) without any difference in gender or age, however. The children receiving melatonin prior to EEG were somewhat younger than those undergoing sleep deprived EEGs (6.3 vs. 7.5 years, $p \leqslant 0.05$) (Fig. 1). There were no significant differences in the proportion of children with a previously established diagnosis of epilepsy (21% in the melatonin group vs. 16% in the sleep deprived group) or number of normal EEG recordings (Table 1).

4. Discussion

The main object of our study was to determine whether melatonin induced sleep is a reliable alternative to partial sleep deprivation without reducing epileptiform discharges in the EEG. Epileptiform discharges were recorded in 33% of the children receiving melatonin before EEG and in 36% of the children that were sleep deprived (n.s.). Wassmer et al. (2001b) reported 37% of seizure activity in the EEG during melatonin induced sleep in children with previously normal standard EEG. In the study by Sander et al. (2012) additional intake of melatonin showed no effect on abnormal findings (i.e., epileptic discharges, focal or generalised slowing) in sleep deprived children. DeRoos et al. (2009)

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Table 2
Mean age, frequency of epileptiform discharges and occurrence of sleep in different age groups of children examined with EEG after melatonin induced sleep versus sleep deprivation.

Age group/variables	Melatonin $n = 129$	Sleep deprivation $n = 113$	p-Value
1–4 years			
n (%)	56 (43)	33 (30)	$\leqslant 0.01$
Mean age, (±SD)	2.8 (±1.0)	1.9 (±0.9)	$\leqslant 0.001$
Epileptiform discharges, n (%)	18 (32)	7 (21)	n.s.
Occurrence of sleep, n (%)	46 (82)	19 (58)	$\leqslant 0.01$
5–8 years			
n (%)	36 (28)	31 (27)	n.s.
Mean age, (±SD)	6.7 (±1.0)	6.1 (±1.0)	$\leqslant 0.05$
Epileptiform discharges, n (%)	13 (36)	10 (32)	n.s.
Occurrence of sleep, n (%)	24 (67)	24 (77)	n.s.
9–12 years			
n (%)	26 (20)	24 (21)	n.s.
Mean age, (±SD)	10.2 (±1.2)	10.5 (±1.2)	n.s.
Epileptiform discharges, n (%)	11 (42)	15 (62)	n.s.
Occurrence of sleep, n (%)	15 (58)	19 (79)	n.s.
13–16 years			
n (%)	11 (9)	25 (22)	$\leqslant 0.01$
Mean age, (±SD)	14.5 (±1.0)	14.0 (±0.8)	n.s.
Epileptiform discharges, n (%)	3 (27)	9 (36)	n.s.
Occurrence of sleep, n (%)	7 (64)	17 (68)	n.s.

n.s. = not significant.

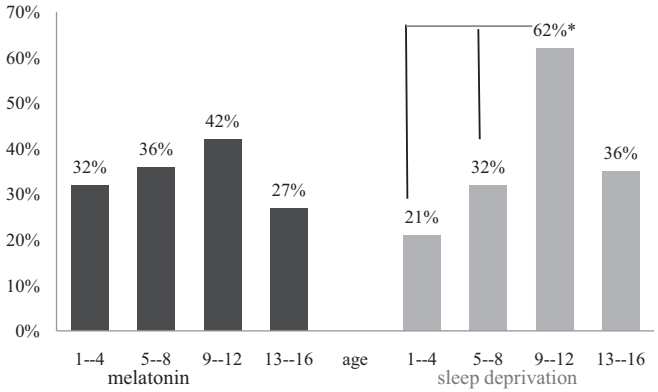

Fig. 2. Distribution of epileptiform discharges (%) in children with melatonin and sleep deprived EEG recordings. Comparison between different age groups. (*$p \leqslant 0.05$).

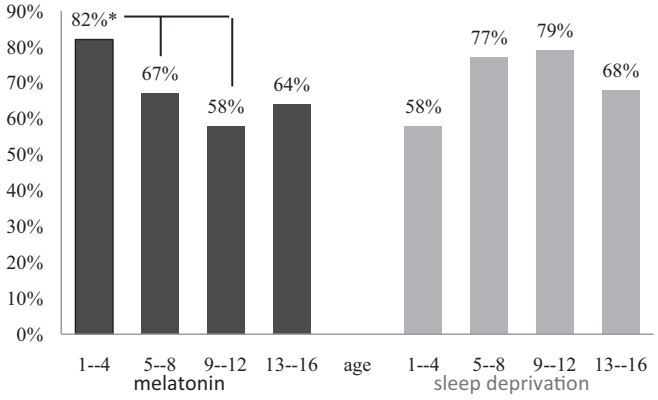

Fig. 3. Distribution of sleep (%) in melatonin induced sleep EEG recordings and sleep deprived EEGs. Comparison between different age groups. (*$p \leqslant 0.05$).

published similar results as ours with a frequency of epileptiform activity of 35–40% in children undergoing routine and sleep deprived EEG with modestly increased frequency of epileptiform activity in sleep deprived EEGs in comparison with routine recordings. These authors recommend using sleep deprivation in children >3 years of age in whom an epilepsy diagnosis is highly suspected after a neurology investigation.

We observed a significantly higher percentage of epileptiform discharges in children 9–12 years old after partial sleep deprivation (62%) in comparison to younger sleep deprived children (Fig. 2). Some types of epilepsies (i.e., awakening epilepsies) are more frequent in this age group (Panayiotopoulos, 2005). Idiopathic generalised epilepsies like juvenile absence epilepsy, juvenile myoclonic epilepsy and epilepsy with grand mal on awakening have a strong age-related onset between 8 and 13 years of age and are also considered more sensitive to be revealed by sleep deprivation (Dinner, 2002; Janz, 2000; Niedermeyer and Lopes da Silva, 2005a). Therefore and in line with our observations, sleep deprivation can still be preferable in older children in order to reveal epileptiform discharges.

In young children, EEG during wakefulness may be nearly impossible to perform and many laboratories favour sleep deprivation (Riviello et al., 2011). On the other hand, sleep deprivation in these children is burdensome for the parents (Wassmer et al., 1999) and not easy to perform properly. Therefore partial sleep deprivation is often used instead of whole night (Gilbert et al., 2004; Panayiotopoulos, 2005). In the present study EEGs after partial sleep deprivation were performed in the morning and EEGs after melatonin intake in the early afternoon. Wassmer et al. (2001b) showed that melatonin was more effective to induce sleep if it was taken in the afternoon in comparison with morning hours. Difference in the time of the day for the EEG recording could therefore theoretically have influenced the results of the present study.

In the present study both children receiving melatonin and those who were sleep deprived obtained sleep in about 70%, corroborating previous studies (Johnson et al., 2002; Wassmer et al., 2000, 2001b). The effect of melatonin as a sleep inducer for EEG in children between 1 and 16 years of age as a whole group have been described, however, without specific notion to age subgroups (Eisermann et al., 2010; Sander et al., 2012; Wassmer et al., 2001b). The development of the child's brain is rapid during this period which is reflected in the EEG. Also epidemiological characteristics and the prevalence of different kinds of epilepsies differ in children 1–16 years of age. Therefore we analysed the EEGs separately in different age groups. In the group of children who got melatonin

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prior to EEG those between 1 and 4 years of age fell asleep more often compared to those between 5 and 12 years of age. A possible explanation could be that the dose of melatonin was not high enough for older children. All children older than 4 years of age got the same dose of 6 mg. Melatonin dosage was based on studies by Wassmer et al. (2001a) who recommended a dose of 2.5–5 mg depending on age. In a Cochrane review (Herxheimer and Petrie, 2002) it is stated that doses between 0.5 and 5 mg have similar effect and that doses higher than 5 mg does not appear to be more effective. The only difference is that 5 mg induces sleep faster than 0.5 mg. The level of endogenous melatonin reaches it peak at approximately 1–3 years of age and thereafter falls gradually during lifetime (Waldhauser et al., 1988). This fact could be an explanation why younger children easier fell asleep than older after melatonin intake and also easier obtained sleep than sleep deprived children from the same age group (Table 2, Fig. 3). Our data in this group, i.e., 1–4 years old children with melatonin versus sleep-deprived EEGs, should be interpreted with some caution primarily because of differences in mean age. In addition, the age distribution was different among children who got melatonin prior to EEG compared to those who were sleep deprived, as a significantly larger proportion of the children undergoing melatonin EEGs were younger (i.e., 1–4 years old; Table 2). This might have influenced the results. A reason for the higher percentage of 1–4 year old children among those who got melatonin is that this is the preferred method of sleep induction in this age group in our laboratory due to the practical difficulties in ensuring proper sleep deprivation. EEG after partial sleep deprivation is still routinely performed in older children, especially in teenagers, who have fewer problems to stay awake during night. This is a potential source of selection bias, and therefore one limitation of this study. Despite this, no differences in occurrence of epileptic discharges between melatonin and sleep deprived EEG were found, neither between children 1–16 years old as a whole group nor between children from different age groups.

The number of EEGs that we defined as unsuccessful was 8% in the melatonin group and 10% in the partially sleep deprived children. In some instances EEGs were impossible to record due to an uncooperative child and in other instances the EEG was impossible to draw any conclusions from because of movement/muscle artefacts and as a consequence high impedance electrode artefacts. In literature reviews unsuccessful EEGs in children has been reported in 4–9% of the recordings which is within the limits of our observations (DeRoos et al., 2009; Olson et al., 2001; Wassmer et al., 2001b). Sander et al. (2012) reported more artefacts and higher number of unsuccessful EEGs, but still not significant, in children who got melatonin prior to EEG in comparison with those who were sleep deprived. Eisermann et al. (2010) found that sleep after melatonin intake was obtained in 80% of the total population and in 72% of patients with severe behaviour problems. We did not separately analyse the sleep inducing effect of melatonin in children with developmental delay and/or behaviour problems as the total numbers were small.

Our study was performed retrospectively which is a limitation. In future prospective studies with the aim to investigate the sleep inducing effect of melatonin and its influence on epileptiform discharges, age-specific analyses should be performed in larger samples, in order to reduce the risk of type II errors. Thus, this type of studies is needed to confirm our observations.

5. Conclusion

This study confirms that melatonin can be reliably used as sleep inducer for EEG recordings in children. Sleep deprivation may not be easy to achieve in young children, and melatonin induction could therefore be advantageous. This is of clinical importance since melatonin intake prior to an EEG recording does not need any special arrangements with the parents before the examination in contrast to sleep deprivation. Sleep deprivation could still be preferable in older children as melatonin probably has less sleep inducing effect in children >4 years of age.

Conflict of interest

None of the authors have potential conflicts of interest to be disclosed.

References

Ashrafi MR, Mohammadi M, Tafarroji J, Shabanian R, Salamati P, Zamani GR. Melatonin versus chloral hydrate for recording sleep EEG. Eur J Paediatr Neurol 2010;14:235–8.
Cortese S, Brown TE, Corkum P, Gruber R, O'Brien LM, Stein M, et al. Reassessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2013;52:784–96.
Degen R. A study of the diagnostic value of waking and sleep EEGs after sleep deprivation in epileptic patients on anticonvulsive therapy. Electroenceph Clin Neurophysiol 1980;49:577–84.
DeRoos ST, Chillag KL, Keeler M, Gilbert DL. Effects of sleep deprivation on the pediatric electroencephalogram. Pediatrics 2009;123:703–8.
Dinner DS. Effect of sleep on epilepsy. J Clin Neurophysiol 2002;19:504–13.
Eisermann M, Kaminska A, Berdougo B, Brunet ML. Melatonin: experience in its use for recording sleep EEG in children and review of the literature. Neuropediatrics 2010;41:163–6.
Gilbert D, DeRoos S, Bare M. Does sleep or sleep deprivation increase epileptiform discharges in pediatric electroencephalograms? Pediatrics 2004;114:658–62.
Giorgi F, Maestri M, Guida M, Di Cosio E, Carnicelli L, Perini D, et al. Controversial issues on EEG after sleep deprivation for the diagnosis of epilepsy. Epilepsy Res Treat 2013;2013:614685.
Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag. Cochrane Database Syst Rev 2002(2):CD001520.
Janz D. Epilepsy with grand mal on awakening and sleep–waking cycle. Clin Neurophysiol 2000;111:103–10.
Johnson K, Page A, Williams H, Wassemer E, Whitehouse W. The use of melatonin as an alternative to sedation in uncooperative children undergoing an MRI examination. Clin Radiol 2002;57:502–6.
Leach JP, Stephen LJ, Salveta C, Brodie MJ. Which electroencephalography (EEG) for epilepsy? The relative usefulness of different EEG protocols in patients with possible epilepsy. J Neurol Neurosurg Psychiatry 2006;77:1040–2.
Marinig R, Pauletto G, Dolso P, Valente M, Bergonzi P. Sleep and sleep deprivation as EEG activating methods. Clin Neurophysiol 2000;111:47–53.
Milstein V, Small JG, Spencer DW. Melatonin for sleep EEG. Clin Electroencephalogr 1998;29:49–53.
Mohammadi MR, Mostafavi SA, Keshavarz SA, Eshraghian MR, Hosseinzadeh P, Hosseinzadeh-Attar MJ, et al. Melatonin effects in methylphenidate treated children with attention deficit hyperactivity disorder: a randomized double blind clinical trial. Iran J Psychiatry 2012;7:87–92.
Sleep and EEG. In: Niedermeyer E, Lopes da Silva F, editors. Electroencephalography: basic principles, clinical applications, and related fields. Philadelphia, USA: Lippincott Williams & Wilkins; 2005a. p. 193–207.
Abnormal EEG patterns: epileptic and paroxysmal. In: Niedermeyer E, Lopes da Silva F, editors. Electroencephalography: basic principles, clinical applications, and related fields. Philadelphia, USA: Lippincott Williams & Wilkins; 2005b. p. 255–80.
Olson DM, Sheehan MG, Thompson W, Hall PT, Hahn J. Sedation of children for electroencephalograms. Pediatrics 2001;108:163–5.
Panayiotopoulos CP. Optimal use of the EEG in the diagnosis and management of epilepsies. The epilepsies: seazures, syndromes and management. 1st ed. Oxfordshire (UK): Bladon Medical Publishing; 2005. p. 304–20.
Sander J, Shamdeen MG, Gottschling S, Gortner L, Gräber S, Meyer S. Melatonin does not influence sleep deprivation electroencephalogram recordings in children. Eur J Pediatr 2012;171:675–9.
Riviello J, Nordli D, Niedermeyer E. Normal EEG and sleep: infants to adolescents. In: Schomer DL, Lopes da Silva FH, editors. Niedermeyer's electroencephalography: basic principles, clinical applications, and related fields. Philadelphia, USA: Lippincott Williams & Wilkins; 2011. p. 166–72.
Waldhauser F, Weiszenbacher G, Tatzer E, Gisinger B, Waldhauser M, Schemper M, et al. Alterations in nocturnal serum melatonin levels in humans with growth and aging. J Clin Endocrinol Metab 1988;66:648–52.
Wassmer E, Quinn E, Seri S, Whitehouse W. The acceptability of sleep-deprived electroencephalograms. Seizure 1999;8:434–5.
Wassmer E, Ross C, Whitehouse W. Therapeutic options for melatonin use in children. Paediatr Perinat Drug Ther 2000;4:45–51.
Wassmer E, Quinn E, Whitehouse W, Seri S. Melatonin as a sleep inductor for electroencephalogram recordings in children. Clin Neurophysiol 2001a;112:683–5.
Wassmer E, Carter P, Quinn E, Welsh G, Seri S, Whitehouse WP. Melatonin is useful for recording sleep EEGs: a prospective audit of outcome. Dev Med Child Neurol 2001b;43:735–8.
Wassmer E, Whitehouse WP. Melatonin and sleep in children with neurodevelopmental disabilities and sleep disorders. Curr Paediatrics 2006;16:132–8.

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